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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,859	06/14/2005	James C. Price	G25-079US	5778

28156 7590 09/04/2008

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EXAMINER	
PALENIK, JEFFREY T	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
09/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,859	PRICE ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *14 June 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Remarks

The Examiner thanks the Applicants for their timely reply filed on 13 February 2008, in the matter of 10/538,859.

Applicants' arguments filed 13 February 2008 have been fully considered but they are not persuasive.

Applicants' election **with traverse** of Group I, claims 1-13, is acknowledged. Applicants traverse the restriction requirement on the grounds that the originally filed claims are sufficiently narrow to allow the Examiner to determine the patentability without being subjected to the serious burden referred to in MPEP §803. Applicants also elect the polymer species combination of cellulose acetate butyrate (CAB) and cellulose acetate phthalate (CAP). The Examiner acknowledges said species election despite the fact that **no formal species election requirement was set forth** by the Office.

Applicants' request for reconsideration of the restriction requirement has been fully considered by the Examiner and is persuasive. Upon further consideration of the claims submitted by Applicants, a new requirement follows. However, the inventions previously listed as Groups I (claims 1-13), II (claims 18-30), III (claims 14-17), IV (claims 31-34), V (claims 35-47), and VI (claims 48-60), still do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same corresponding technical feature(s). There is no special technical feature since the journal article to Obeidat et al., expressly teaches the invention of claim 1, wherein the claimed microspheres comprise a core-concentrated active ingredient which is dispersed amidst two

pH-sensitive, hydrophobic polymers, an organic solvent, a second solvent and a surfactant (see *J. Microencapsulation,* Jan. 2003, (20), No. 1, pp. 57-65).

Applicants' provisional elections of Group I (claims 1-13) and the respective species, as discussed above, stand. Furthermore, claim 3 remains provisionally withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention and species, there being no allowable generic or linking claim. Applicants timely traversed the restriction (lack of unity) between the microsphere composition and the distinct compositions comprising said particle composition. The remaining claims 1, 2 and 4-13 are presented and represent all claims under consideration.

Information Disclosure Statement

An Information Disclosure Statement filed 14 June 2005 is acknowledged and has been reviewed.

Specification

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2 and 4-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "highest" in claim 1 is a relative term which renders the claim indefinite. The term "highest" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The parameter rendered indefinite by use of the above term is the concentration of active ingredient which is present within the core of the microsphere composition. Herein, and for the purposes of examination on the merits, the Examiner broadly and reasonably interprets any focused or loaded amount of active agent as comprising the point where the active concentration is highest in the particle.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2 and 4-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Obeidat et al. (*Journal of Microencapsulation*) in view of Liu et al. (*Journal of Pharmacy and Pharmacology*).

The instant claims are directed to microspheres comprising an active ingredient dispersed within a polymeric composition comprising two individual hydrophobic, pH-sensitive polymers, which are themselves dispersed in an organic solvent, further mixed with an additional solvent and a surfactant. The instant claim 1 recites limitations to: 1.) the concentration of the second polymer with respect to the total weight of both polymers, 2.) the microsphere diameter, 3.) the weight range of active ingredient in the composition, and 4.) the core of the microsphere such that the core contains a loaded amount, as discussed above. Claim 2 recites compositional limitations to the first and second polymers (e.g. esterified celluloses), the organic solvent (e.g. a ketone), the second solvent (e.g. a mineral oil) and the surfactant (e.g. sorbitan sesquioleate). Claim 4 further limits the first and second polymers of claim 1 to combinations and mixtures of cellulose based compounds. Claim 5 further limits the first polymer to CAB and the second polymer to CAP. Claims 6 and 7 further limit the total polymer concentration based on the concentration of CAP in the composition. Claim further limits the size of the microspheres. Claim 9 further limits the ranges of both polymers and the particle size. Claims 10 and 11 recite limitations to the active ingredient (i.e. the bronchodilator theophylline). Claim 11 further specifies both acetone and sorbitan sesquioleate. The

limitation of claim 12 "wherein upon distribution of the microspheres into an aqueous environment…" is considered by the Examiner as a recitation of intended use, which per MPEP §2111, hold no patentable merit since said use does not impact the instantly claimed composition. The limitation of claim 12 wherein "substantially all of the active ingredient is released … between 12 to 24 hours" is viewed by the Examiner as being a property which is inseparable from the instantly claimed composition (see MPEP §2112.01 (II)). Claim 13 recites limitation to the one in claim 12 where substantially all of the second polymer will dissolve when all of said polymer has been released when exposed to an aqueous environment. Again, the limitations are considered by the Examiner as reciting intended use of the microspheres (e.g. exposure to an aqueous environment), which result in the exhibition of physical properties which are inseparable from the chemical composition. Thus, both claims 12 and 13 are not considered by the Examiner to further limit the composition of claim 5.

Obeidat et al. teach matrix microsphere preparations which employ two different polymers of cellulose acetate butyrate (e.g. CAB381-2 and CAB381-20) as the hydrophobic, pH-sensitive polymers and theophylline as the active agent (see pp. 57-58; *Introduction*). Sorbitan sesquioleate (e.g. surfactant), the organic solvent acetone (e.g. organic solvent), heptane (e.g. additional solvent) and mineral oil (e.g. additional solvent) are all taught (see *Materials*, pg. 58). Microspheres with 33% theoretical drug loading of anhydrous theophylline core material are taught (see *Abstract*). The second of the two polymers (e.g. CAB381-20) is taught as being present at 7.25-9% (w/w) in the organic phase whereas the total percent contribution of the two polymers together range from about

15-24% (w/w) (see pg. 58; *Preparation of microspheres*). Particle size distribution is taught as ranging from 106-710 microns (pg. 59; *Particle size distribution*).

Obeidat does not expressly teach using cellulose acetate phthalate as the second hydrophobic polymer in the composition.

Liu et al. teach dual polymer suspensions of microparticles for controlled release of an active agent, wherein the preferred polymer combination taught as comprising a ratio of 0.4:1.6 (e.g. 20%:80%) cellulose acetate phthalate/cellulose acetate butyrate mixture (Abstract). The microparticles are further taught as being prepared by using a modified solvent evaporation method comprising acetone and alcohol. The microparticles which resulted were sieved through a 180 micron filter.

Liu does not teach the active agent theophylline, the sorbitan sesquioleate surfactant or an oil based second solvent.

In view of the combined teachings of the prior art, one of ordinary skill in the pharmaceutical art, at the time of the invention, would have been motivated to disperse an active agent amidst a combination of cellulose acetate butyrate and cellulose acetate phthalate (e.g. two pH-sensitive hydrophobic polymers) in order to achieve the instantly claimed microsphere composition. Such would have been obvious in the absence of evidence to the contrary since both Obeidat et al. and Liu et al. overlap in their teachings of controlled release, microparticle suspension dosage forms comprising dual, pH-sensitive hydrophobic polymers. The two teachings also overlap in that both employ solvent

evaporation methods in order to disperse the active agent in the polymeric composition wherein both contain multiple active agents which are physically separated from one another within the same dosage. Furthermore, one of ordinary skill in the art would have been motivated to use the CAP/CAB polymer solution practiced by Liu et al. for the CAB/CAB polymer solution employed by Obeidat particularly since Obeidat teaches that the polymer solution could be predictably optimized by adjusting the viscosity of the polymer solutions on the basis of their viscosity and molecular weight properties (Abstract).

Therefore, a person of ordinary skill in the art would have a reasonable expectation of success in modifying the dosage form practiced by Obeidat in view of the dual polymer solution practiced by Liu et al. since the combined teachings disclose the instantly claimed the dispersed active, dual-polymer microsphere composition.

All claims have been rejected; no claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615